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Molecular bases of brain preconditioning

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Abstract

© 2017 Deryagin, Gavrilova, Gainutdinov, Golubeva, Andrianov, Yafarova, Buravkov and Koshelev. Preconditioning of the brain induces tolerance to the damaging effects of ischemia and prevents cell death in ischemic penumbra. The development of this phenomenon is mediated by mitochondrial adenosine triphosphate-sensitive potassium (KATP+) channels and nitric oxide signaling (NO). The aim of this study was to investigate the dynamics of molecular changes in mitochondria after ischemic preconditioning (IP) and the effect of pharmacological preconditioning (PhP) with the KATP+-channels opener diazoxide on NO levels after ischemic stroke in rats. Immunofluorescence-histochemistry and laser-confocal microscopy were applied to evaluate the cortical expression of electron transport chain enzymes, mitochondrial KATP+-channels, neuronal and inducible NO-synthases, as well as the dynamics of nitrosylation and nitration of proteins in rats during the early and delayed phases of IP. NO cerebral content was studied with electron paramagnetic resonance (EPR) spectroscopy using spin trapping. We found that 24 h after IP in rats, there is a two-fold decrease in expression of mitochondrial KATP+-channels ($p = 0.012$) in nervous tissue, a comparable increase in expression of cytochrome c oxidase ($p = 0.008$), and a decrease in intensity of protein S-nitrosylation and nitration ($p = 0.0004$ and $p = 0.001$, respectively). PhP led to a 56% reduction of free NO concentration 72 h after ischemic stroke simulation ($p = 0.002$). We attribute this result to the restructuring of tissue energy metabolism, namely the provision of increased catalytic sites to mitochondria and the increased elimination of NO, which prevents a decrease in cell sensitivity to oxygen during subsequent periods of severe ischemia.

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Keywords

ATP-sensitive potassium channels, Ischemic preconditioning, Mitochondria, Neuroprotection, Nitric oxide

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